# PREDICTION OF CALCIUM OXALATE STONE RISK WITH INTERVENTIONS

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# The challenge in appraising symptomatic renal stone risk

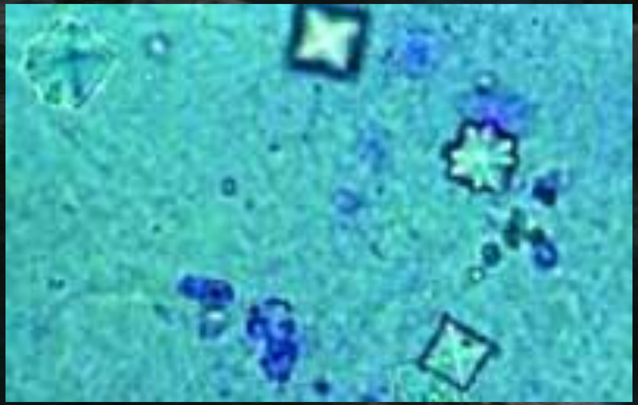
*Altered Gravity Fields*

*Hostile Closed Environment*

*Radiation*

*Isolation/Confinement*

*Distance from Earth*

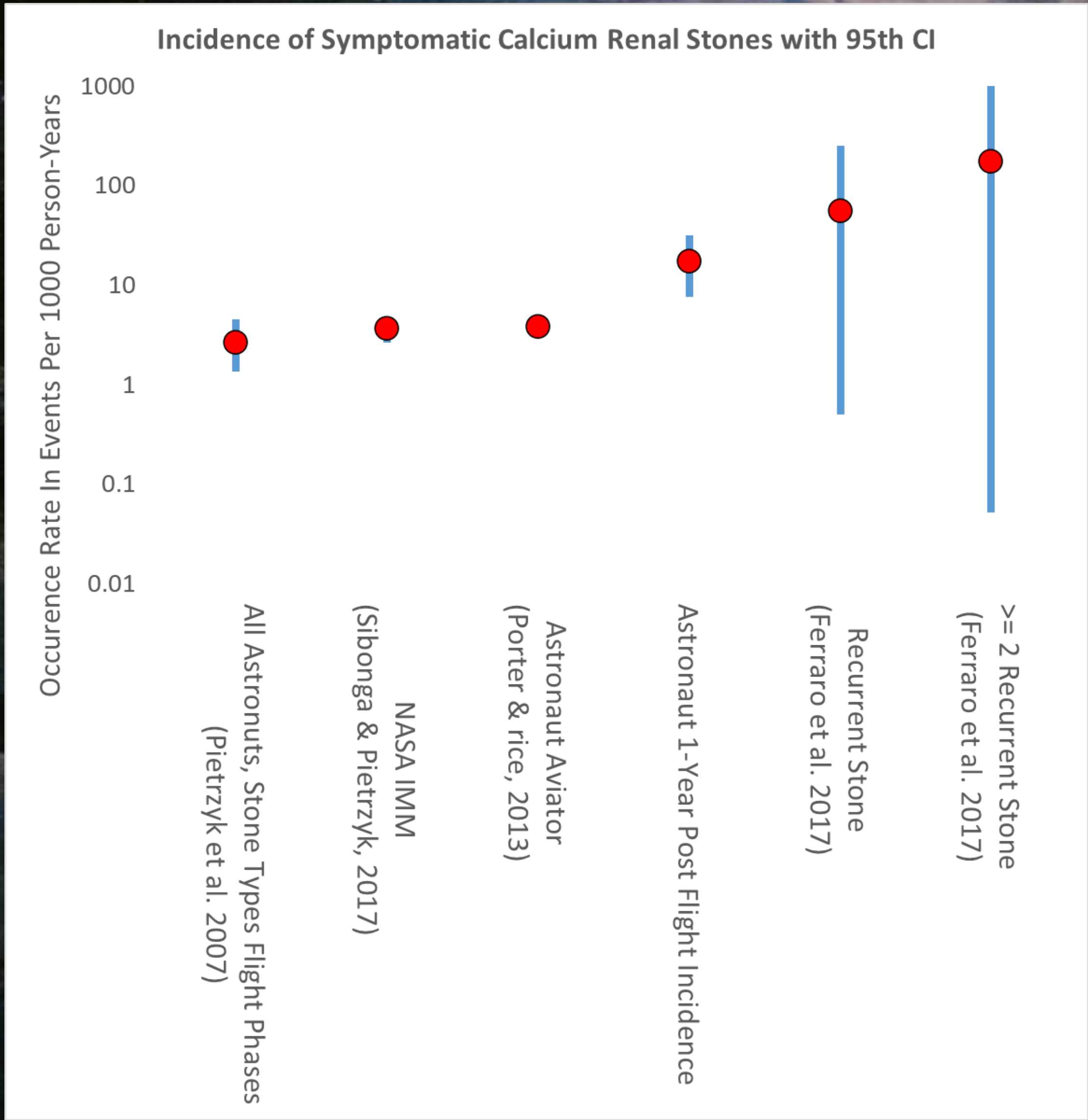


https://www.nasa.gov/centers/marshall/news/background/facts/renal.html

- Unloading → bone demineralization
- Increased resorption of calcium

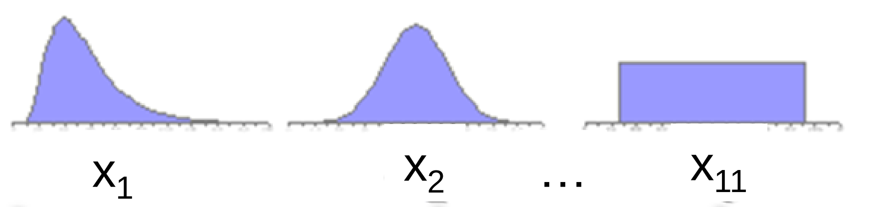
- Exercise → promotes osteocyte negative resorption – only a moderate effect on serum calcium

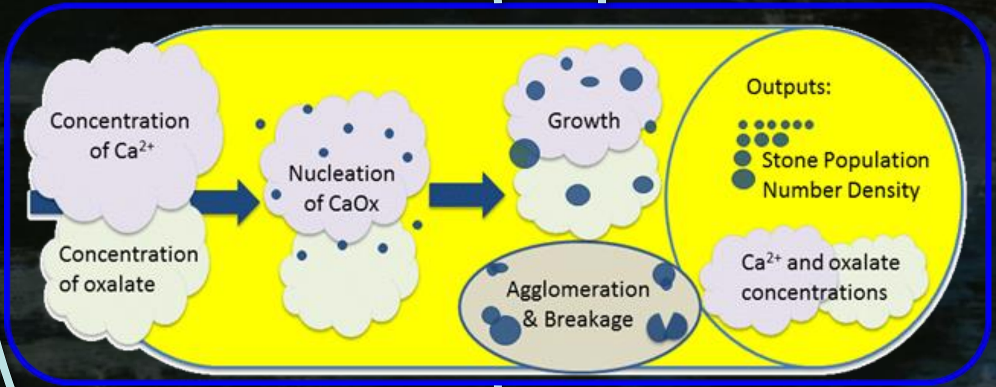
- Result: Elevated urine calcium and the prospect of increased renal stone presentation



# CCMP Renal Stone Risk Model

1517 Urine Chemistries – 11 Constituent Measures



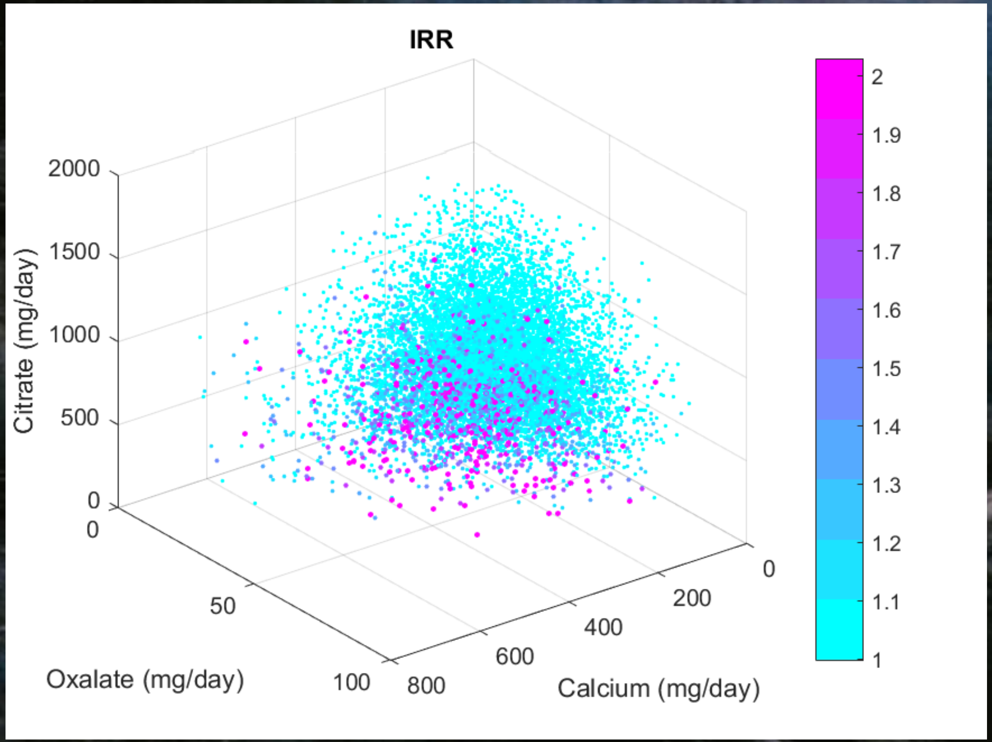




Population Balance Equation (PBE) Model - Kassemi & Thompson (2016)

Urine Speciation with the Joint Expert Speciation System (JESS) Rodgers, Allie-Hamdulay, & Jackson (2006)

Monte Carlo Output

- **IRR – Incidence Risk Ratio relative to pre-flight incidence rate**



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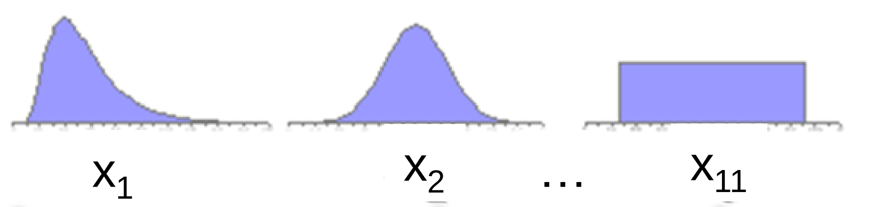


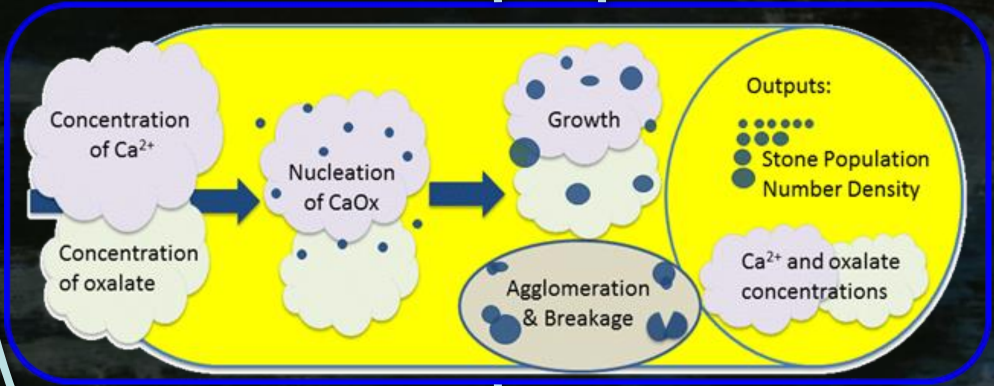


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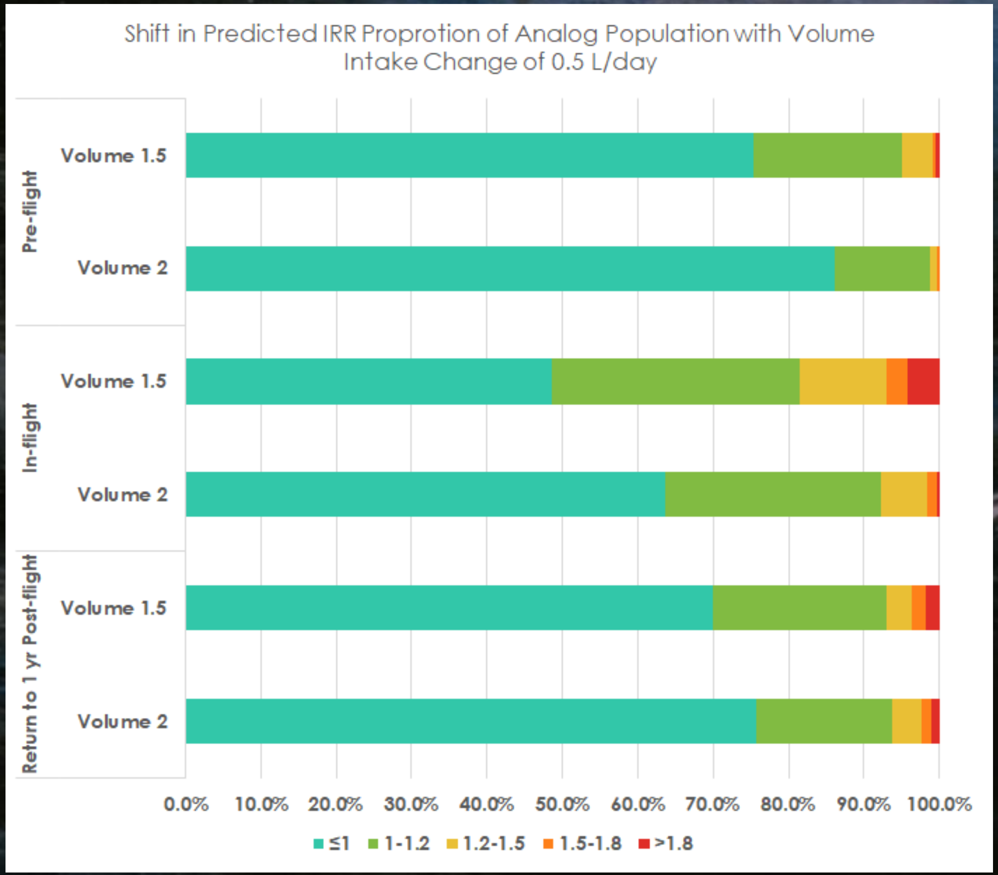
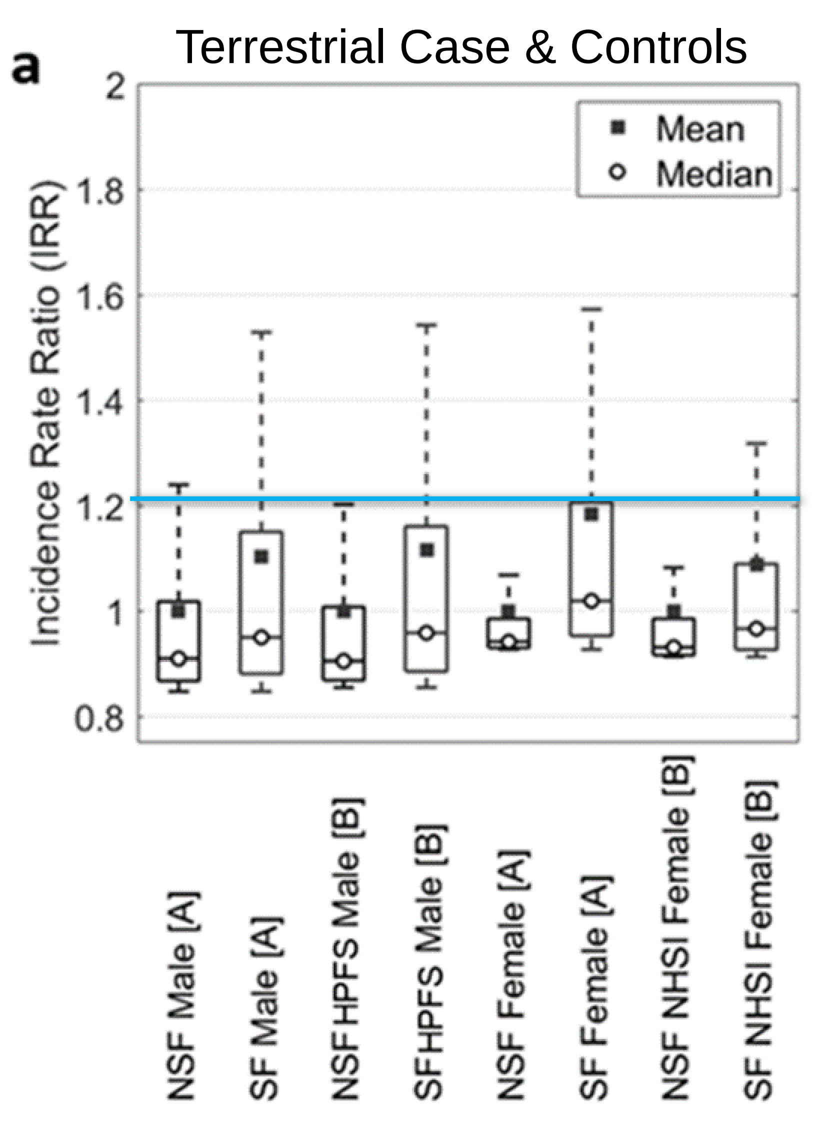
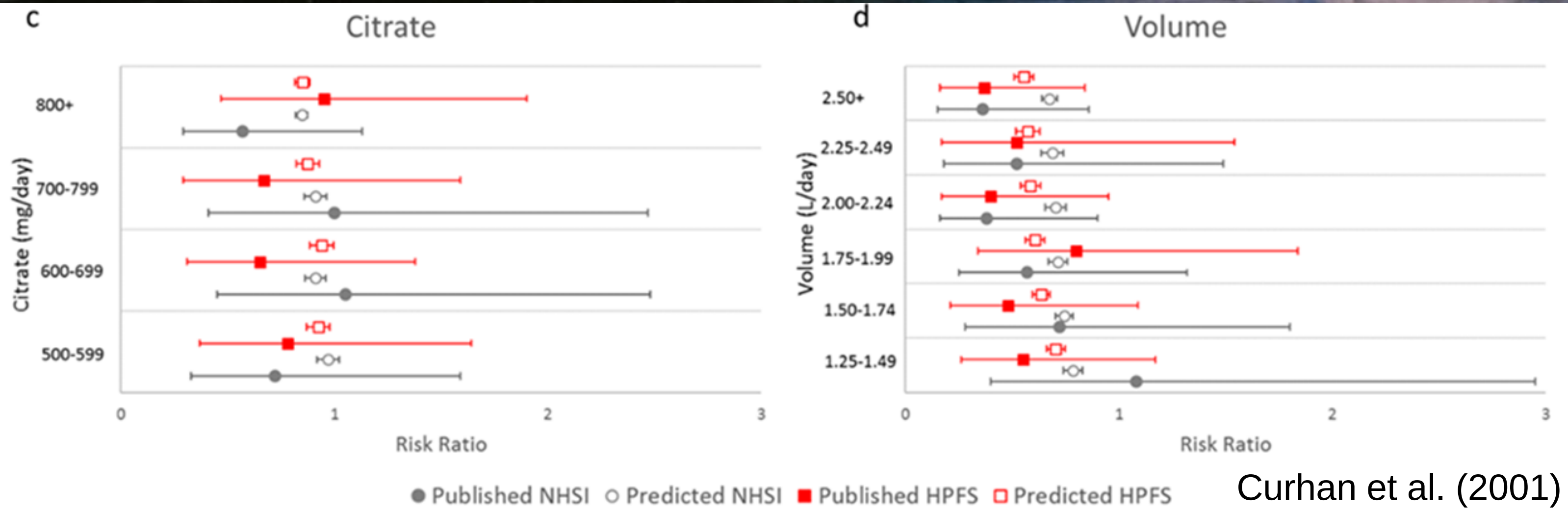
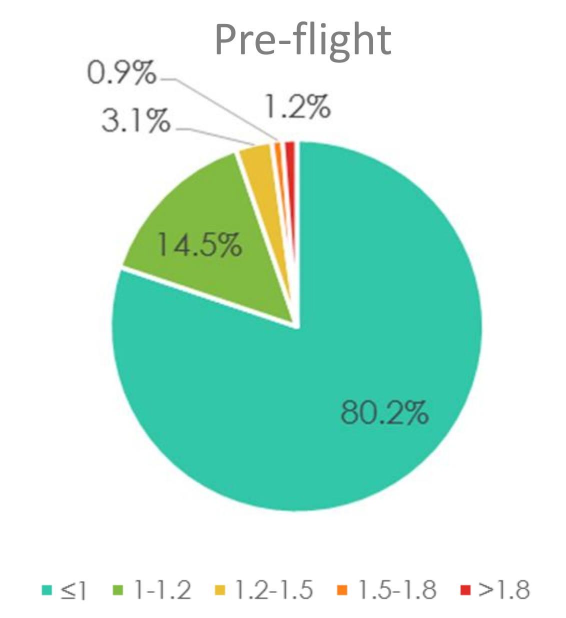


# GRC Model Characterization



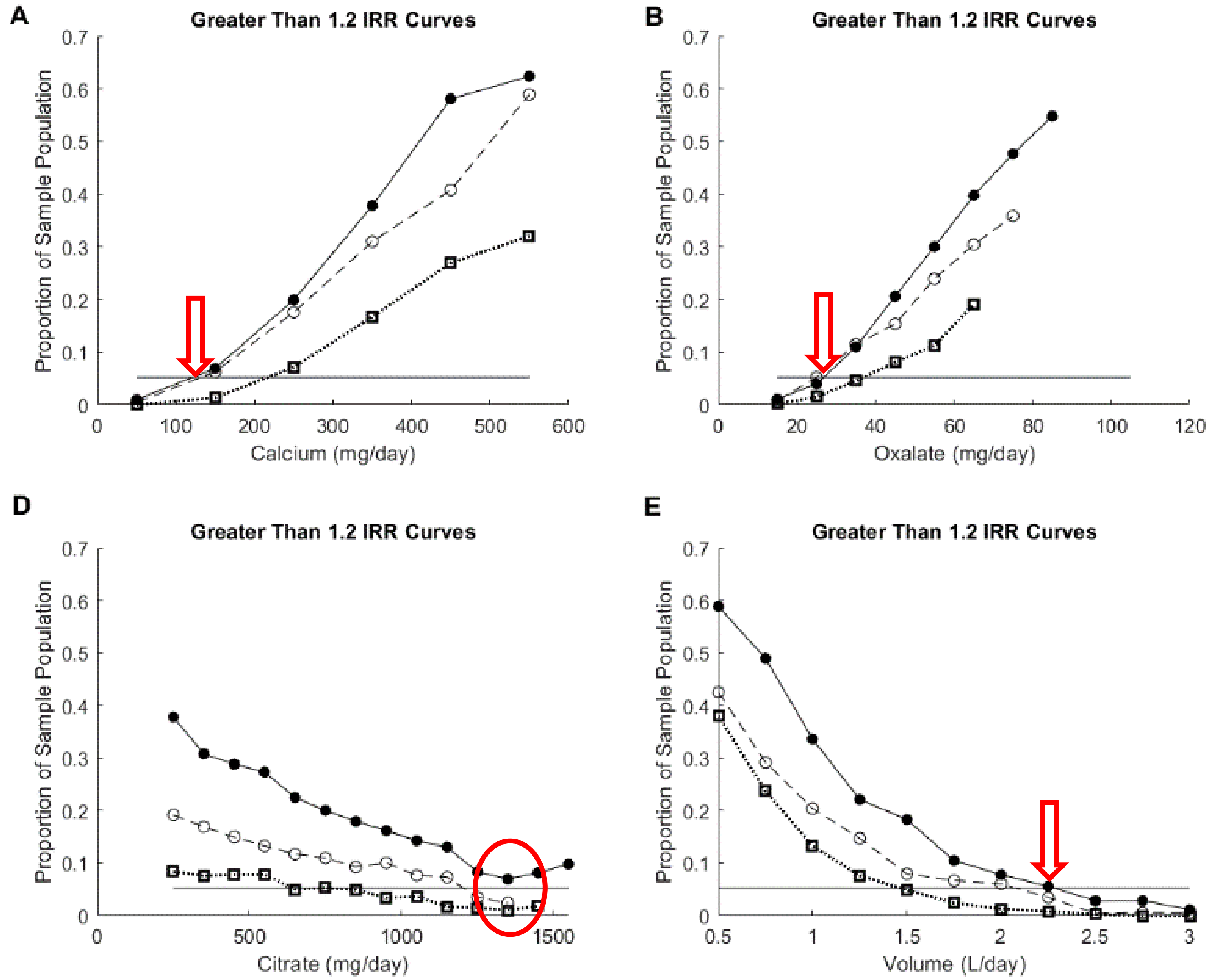




Curhan et al. (2001)




- **Goodenow-Messman et al., NPJ Microgravity (2022)**
- **Natural IRR cutoff of 1.2 – 95% of pre-flight astronauts fall at or below this value**
- **Seems to correspond to the terrestrial case and control simulations**

# Where do astronauts fall on this threshold? – Single factor




Example in-flight recommendations:

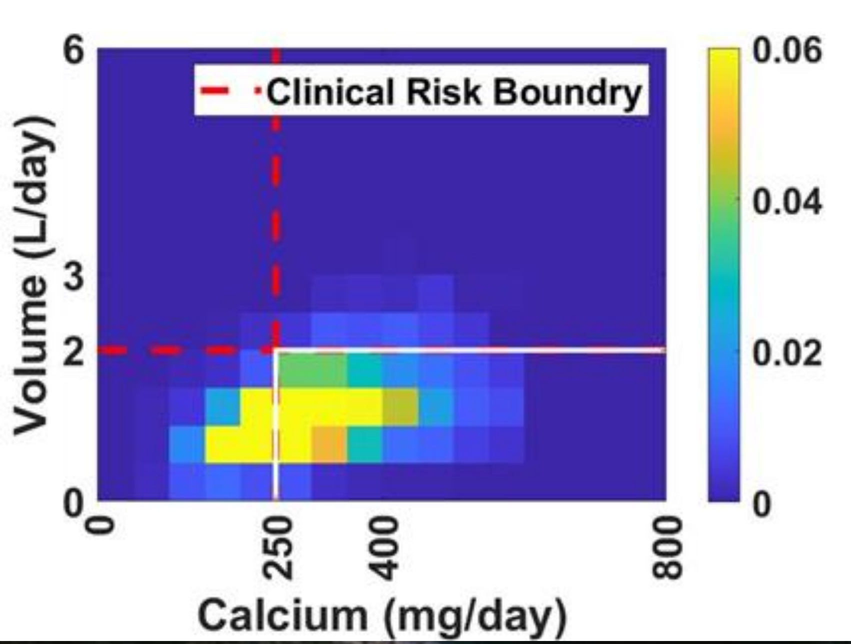
- Fluid intake 2.95-3.15 L/day (output 2.25 L/day)
- Reduce Ca excretion to <150 mg/day

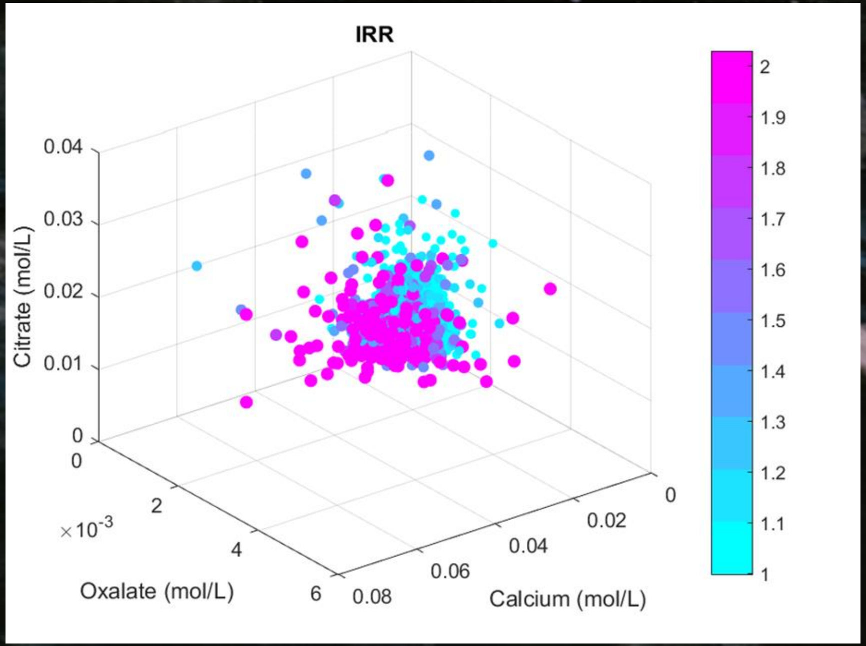
# Considering multiple mitigations

- **We postulated that risk can be returned to pre-flight levels by combining mitigations at a lower burden to each countermeasure**

- **> 98% of simulated populations exhibit IRR<1.2 when**
  - Increase fluid intake by 0.5 L/day + Bisphosphonates (reduce calcium excretion by ~45 mg/day) + Exercise
  - Increase fluid intake by 0.5 L/day + Control oxalate excretion (diet) to ~35 mg/day

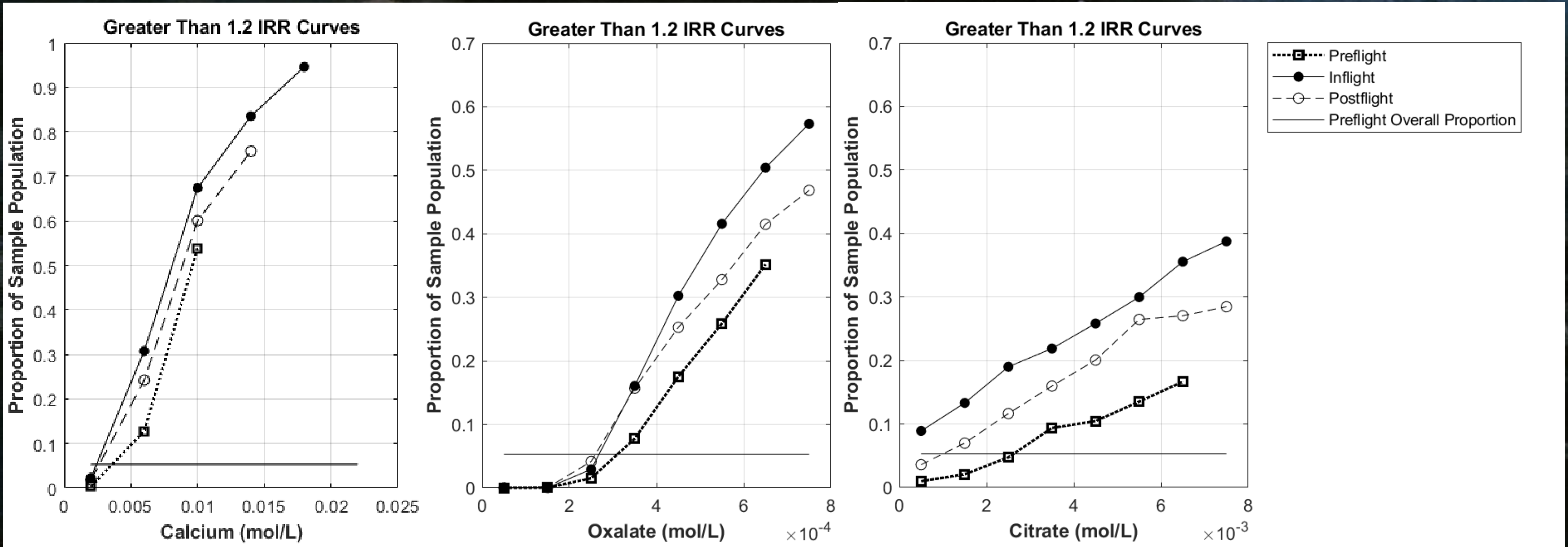
Proportion of the simulated in-flight astronaut population with IRR > 1.2



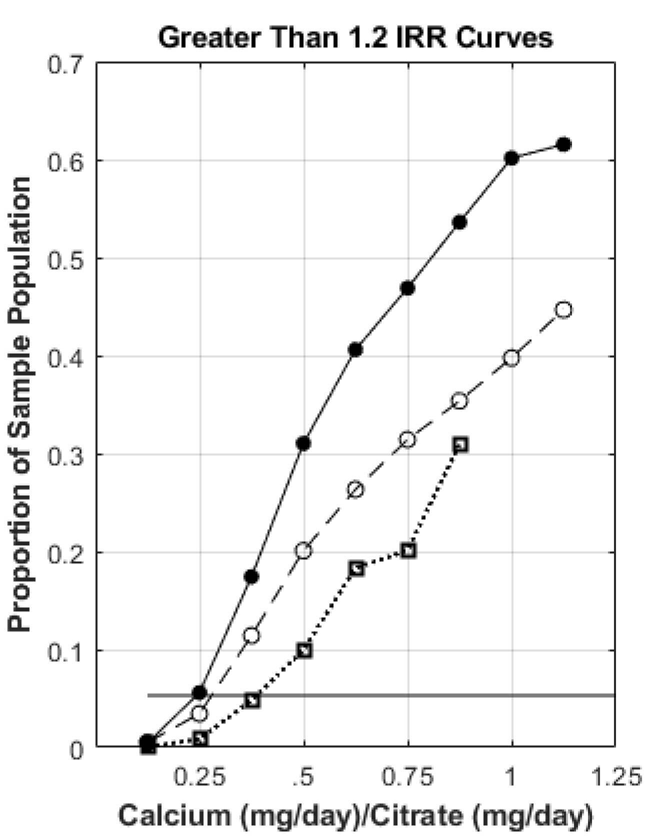



# Normalizing By Urine Output

- As expected, normalizing by urine output results in narrower variation between concentrations of promoters near the preflight IRR threshold
- Illustration of citrate's maximized inhibition effect (*low V→ high concentration*)
- Potentially useful in assessing individual risk reducing fluid intake increase for measured 24-hr Ca, Ox.



# Conclusions and future work




Similar to normalizing with volume, other inhibitors and constituents can be evaluated

- **Demonstrated a means of quantifying relative renal stone risk and how mitigation strategies may alter that risk**
- **Although premised on ISS shuttle data, this approach is extensible to informing lunar and Martian missions**
- **Assumption of fixed in-mission risk will be investigated in future analyses**
- **Ongoing efforts to interface the model with MEDPRAT**

# Thank you

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